UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/282,239	03/31/1999	STEVEN A. GOLDMAN	19603/1426	8339

7590 12/23/2009

MICHAEL L GOLDMAN ESQ
NIXON HARGRAVE DEVANS & DOYLE LLP
CLINTON SQUARE PO BOX 31051
ROCHESTER, NY 14603

EXAMINER	
HUTSON, RICHARD G	
ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
12/23/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/282,239	GOLDMAN ET AL.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25,26 and 29-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25,26,29-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's cancellation of claim 45 and amendment of claims 25, 26, 29, 30, 42-44, in the paper of 9/10/2009, is acknowledged. Claims 25, 26 and 29-44 remain at issue and are present for examination.

Applicants' arguments filed on 19/10/2009, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 42-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection of claims 42-45 under this statue remains because the recitation "...wherein 66.3 +/- 6.8% of cells in the enriched or purified preparation mature into O4-IR oligodendrocytes when cultured in the presence of 5% FBS/IGF-1." is not supported by applicants specification at the time of filing and is thus considered new matter.

Specifically applicants recitation of "preparation mature into O4-IR oligodendrocytes " is considered new matter for the reasons previously discussed. As previously stated in the office action of 3/10/2009, it would appear at best the only association that can be made with respect to 66.3 +/- 6.8% is "O4-IR cells". Support for anything beyond such is considered new matter, which includes "O4-IR oligodendrocytes".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 25, 26 and 29-41 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Rao et al. (U.S. Patent No. 6,361,996 B1).

This rejection which was stated in the previous office action as it applied to claims 25, 26 and 29-41. In response to the rejection applicants have amended claims 25, 26, 29, 30 and continue to traverse the rejection as it applies to the newly amended claims.

For applicants convenience the original rejection is repeated herein:

Rao et al. teach an isolated, pure (enriched or purified) and homogeneous population of lineage-restricted oligodendrocyte-astrocyte precursor cells which are

capable of self-renewal and differentiation into oligodendrocytes and astrocytes and methods of generating, isolating and culturing such oligodendrocyte-astrocyte precursor cells. The specific pure homogeneous population of cells isolated by Rao et al. is illustrated in Figure 1 (See specifically cell type –14, and the supporting text) and while Rao et al. specifically teach as an example said pure (enriched or purified) homogeneous preparation of cells as isolated from rat, Rao et al. point out that the invention encompasses all mammalian neuroepithelial stem cells and is not limited to neuroepithelial stem cells from the rat. Mammalian neuroepithelial stem cells can be isolated from human and non-human primates, equines, canines, felines, bovines, porcines, ovines, lagomorphs, and the like. Thus, Rao et al. anticipates those claims to an enriched or purified preparation of human mitotic oligodendrocyte progenitor cells, the majority of which mature into oligodendrocytes, wherein an oligodendrocyte specific promoter (CNP2) is transcriptionally active in the oligodendrocyte progenitor cells.

The preparation taught by Rao is such that a cyclic nucleotide phosphodiesterase 2 promoter is inherently transcriptionally active in all cells of the enriched or purified preparation. This is evidenced by the reference Scherer et al. (Neuron Vol 12, pp 1363-1375, June 1994, see applicants IDS) who teach the differential cellular and temporal regulation of the 2',3'-cyclic nucleotide 3'-phosphodiesterase gene (CNP)and teach that the 2',3'-cyclic nucleotide 3'-phosphodiesterase II promoter is transcriptionally active in oligodendrocytes, Schwann cells and many additional tissues and appears before the appearance of mature

oligodendrocytes, in oligodendrocyte precursor cells early in brain development (See page1365-1367, Figures 4 and 5 and supporting text).

Claims 25, 26 and 30, which are drawn to the preparation of oligodendrocyte progenitor cells of claim 29 are included in this rejection because these product-by-process like limitations ("from a post-natal human" for claim 25 and "from an adult human" for claim 26, fetal human) do not change the oligodendrocyte progenitor cells of claim 29. Rao further teach that a better understanding of a number of tumors and other diseases in humans could be facilitated by a better understanding of these cell types and the ability to isolate and grow these mammalian cells in vitro, which allows for the possibility of using such stem cells to treat neurological disorders in mammals, particularly humans. Further, such mammalian neuroepithelial stem cells can be used therapeutically for treatment of certain diseases, e.g. Parkinson's Disease, such as by transplantation of such cells into an afflicted individual. Moreover, such cells can still further be used for the discovery of genes and drugs that are useful for treating certain of these diseases.

One of ordinary skill in the art at the time of filing would have been motivated to use the methods taught by Rao et al. to isolate an enriched or purified preparation of human mitotic oligodendrocyte progenitor cells from humans so that these pure cell preparations could be used to treat neurological disorders in humans, such as Parkinson's Disease, such as by transplantation of such cells into an afflicted individual. This motivation is suggested by Rao et al. and the reasonable expectation of success

comes from the results of Rao et al. who successfully isolated such an enriched or purified preparation of mitotic oligodendrocyte progenitor cells from rat.

Applciants Argument:

It is noted that applicant's argument presented in the paper of 9/10/2009, is much like that presented by applicants in the paper of 10/27/2008.

Applicants continue to give applicants interpretation of the '996 patent and applicants submit the '996 patent discloses multipotential neuroepithelial stem cells and lineage-restricted astrocyte/oligodendrocyte precursor cells. In particular, applicants submit that after differentiation, in Example 14, the proportion of differentiated cells was 30% oligodendrocytes, 50% astrocytes, and 20% $A2B5^+$ cells.

Applicants continue to submit that similarly, Example 15 of the '996 patent, the $A2B5^+$ cells predominantly differentiate into cells with a type-2 astrocyte phenotype and this is entirely consistent with the previously submitted Second Declaration of Mahendra S. Rao, M.D., Ph.D. Under 37 C.F.R. § 1.132 ("Second Rao Declaration").

Applicants continue to submit that this bias of the '996 patent's astrocyte/oligodendroctye progenitor to differentiate to astrocytes clearly distinguishes them from the presently claimed oligodendrocyte progenitor cells, the majority of which mature into oligodendrocytes.

Applicants continue to point out that it is important to note that multiple pathways to generate post-mitotic, mature oligodendrocytes, have been described and applicants again summarize these as they have previously done.

Applicants continue to focus on those comments of the previous office action which states that the previous claims are anticipated by Examples 7 and 15 of the '996 patent, as according to the PTO, these examples must produce an intermediate between the '996 patent's oligodendrocyte-astrocyte precursor cells and fully differentiated cells.

Applicants continue to submit that the PTO particularly relies on Example 7's mention of cells that appeared to have a different morphology than the oligodendrocyte type-2 astrocyte progenitors or mature oligodendrocytes in asserting anticipation.

Applicants continue to disagree with this argument on two bases. Firstly, applicants continue to submit that these examples involve work with rat cells - not human cells. As previously, this response is recognized, however, not found persuasive on the basis that as previously stated, those claims drawn to the preparation of oligodendrocyte progenitor cells are included in this rejection because these product-by-process like limitations ("from a post-natal human" for claim 25 and "from an adult human" for claim 26) do not change the oligodendrocyte progenitor cells of claim 29. Further applicants are reminded that the current rejection is a 102/103 type rejection and while the origin of the cells taught by Rao et al. may be rat, applicants are reminded that one of skill in the art would be motivated to isolate the same cell population from

human sources. Applicants respond to this by submitting that not only did Rao et al. not teach such from human, but they did not teach the claimed cell population from humans. In response to this position, it is believed that Rao et al. does in fact teach this cell population of enriched or purified preparation of human mitotic oligodendrocyte progenitor cells, wherein the majority of cells in the enriched or purified preparationdifferentiate into O4 oligodendrocytes under the defined culture conditions and further develop into galactocerebroside positive oligodendrocytes in the defined culture conditions for the reasons previously made of record. While the specific culture conditions referred to in applicants claim may not used in the methods taught by Rao et al., it remains that Rao et al. have taught an enriched or purified preparation of the claimed population of mitotic oligodendrocyte progenitor cells.

Secondly applicants continue to submit that the mention of cells having a morphology that is different than the oligodendrocyte type-2 astrocyte progenitors or mature oligodendrocytes does not mean that those additional cells are the claimed oligodendrocyte progenitor cells. Applicants continue to submit that the PTO's point is entirely speculative and is contrary to what Dr. Rao said in his second declaration and in taking this position, the previous Examiner's Answer is impermissibly ignoring the testimony of Dr. Rao who is in a far better position to know what cell types his work made and did not make. Applicants argument is again acknowledged, however, not found persuasive on the basis that as previously stated it is a reasonable and logical assertion that the cell type which is at the heart of applicants invention is an intermediate between the cell type 14 and 18 of Rao et al. and it must have existed in

the preparations of Examples 15 and 7. Applicants have submitted that there is no evidence of such in the presentation of Dr. Rao's declaration, however, this is contrary to the teaching of Rao et al. as presented previously and below. The office is not ignoring the testimony of Dr. Rao, but rather the office is considering exactly what Dr Rao is testifying to and considering this in light of the evidence based upon the teaching of Rao et al.

Applicants continue to submit that given Rao's clear teaching that his oligodendrocyte-astrocyte precursor cells have an astrocytic bias, it is not apparent how these cells can be regarded as the same as the claimed enriched or purified preparation from which a majority of the cells mature into oligodendrocytes. In any event, applicants submit that the claims have been amended to recite the conditions under which a majority of the cells in the enriched or purified preparation can mature into oligodendrocytes (i.e. cultured in 5% FBS/IGF-1). Since neither these conditions, let alone the result that a majority of the cells of the enriched or purified preparation mature into oligodendrocytes are taught by Rao, this reference can hardly be said to teach or render obvious the claimed invention.

Applicant's amendment of the claims and applicants argument continue to be acknowledged and has been carefully considered, however, continues to be found nonpersuasive for the reasons previously made of record in the previous office actions and the previous examiners answer and for those reasons discussed above and below.

It is noted that applicants have amended the claims to recite "an enriched or purified preparation of human mitotic oligodendrocyte progenitor cells, "wherein the

majority of cells in the enriched or purified preparation differentiate into O4 positive oligodendrocytes when cultured in PDGF, FGF2, and NT3, and further develop into galactocerebroside positive oligodendrocytes in the presence of 5% FBS/IGF-1, ..." thus inserting the conditions by which the cells differentiate into O4-positive oligodendrocytes.

As previously stated if one considers that applicants claims are directed to an oligodendrocyte-specified progenitor cell which is "unipotential" such that it only gives rise to oligodendrocyte cells and not to other types of cells, such as astrocytes, then this "further specified oligodendrocyte-specified progenitor cell" continues to be anticipated by Rao et al. in its preparations of examples 15 and 7. As previously stated, in the previous office actions, each of these example preparations start with NEP-derived A2B5+ cells and allow these progenitors to develop to oligodendrocytes. Thus, the NEP cells differentiated to cell type 14 (as per Figure 1) and further differentiated to cell type 18 (as per Figure 1). Thus an intermediate between the cell type 14 and 18 must have existed in the preparations of Examples 15 and 7.

Previously relative to this argument, applicants submitted and applicants continue to submit that that Dr. Rao is not aware of any evidence that the astrocyte/oligodendrocyte precursor cells of the '996 patent generated mature oligodendrocytes by way of an intermediate oligodendrocyte-specific precursor and applicants further presented Gregori et al., J Neurosci. 22(1):248-256 (2002) as suggesting that the '996 patent describes a glial progenitor that gives rise to a more restricted astrocyte/oligodendrocyte precursor that still directly makes predominantly

astrocytes and a small minority of oligodendrocytes. Thus, applicants submitted that cells in the '996 patent's pathway to oligodendrocyte production are bi- potential astrocyte/oligodendrocyte progenitor cells that have strong astrocytic bias. Applicants continue to submit that these cell types are very different from the claimed oligodendrocyte-specified progenitor cells of the present application.

As in the previous responses to this argument, if one considers that the claimed progenitor cell must be unipotential, such that it only differentiated into an oligodendrocyte cell, (that is an intermediate between cell type 14 and cell type 18) then contrary to the declaration of Dr. Rao, there is evidence of the existence of such a cell type. This evidence is found in Example 7 of the Rao et al. patent. Neither applicant's response of 10/27/2008, 12/18/2008, nor that 9/10/2008, have addressed this previously made point.

As demonstrated in example 7 of Rao et al., NEP cells grown on fibronectin in NEP medium for 5 days according to the procedure of Example 1 were harvested by trypsinization and replated on laminin-coated plates in neuroepithelial culture (NEP) medium without the addition of CEE for 5-10 days. Differentiating NEP cells were then labeled, according to the procedure of Example 4, with markers previously identified as being expressed on oligodendrocytes and their precursors: A2B5, GalC, O1, and O4. Three days after replating NEP cells, a subset of the cells began to express A2B5 immunoreactivity. A2B5 immunoreactive cells initially did not express detectable levels of GalC, O4, and O1 immunoreactivity. These cells correspond to the Figure 1, cell type 14 . After an additional three days in culture, however, “GalC immunoreactive cells

could be seen, which cells also expressed A2B5 immunoreactivity". Such cells appeared flattened and did not have the characteristic morphology of oligodendrocyte-type 2-astrocyte (O2A) progenitors or mature oligodendrocytes. Longer periods in culture, however, allowed more mature-looking oligodendrocytes with a small body and extensive processes to develop. These cells expressed O1 and GalC immunoreactivity, markers characteristic of differentiated oligodendrocytes. These cells which "appeared flattened and did not have the characteristic morphology of oligodendrocyte-type 2-astrocyte (O2A) progenitors or mature oligodendrocytes" are evidence of the existence of an intermediate between cell type 14 and cell type 18 of Figure 1. As stated by Rao et al., the pattern of antigen expression further suggests the existence of a dividing oligodendrocyte precursor that subsequently generates oligodendrocytes, as has been described from spinal cord cultures from older embryos. It is this identified cell type that continues to anticipate applicants claimed cells and applicants have not addressed this point made in the previous office action of 10/27/2008 or that of 9/11/2009.

Given the importance in isolating oligodendrocyte progenitor cells to the understanding of how multipotent neuroepithelial stem cells become restricted to the various neuroepithelial derivatives, one of skill in the art would have been motivated to isolate the cells identified by Rao et al. which "appeared flattened and did not have the characteristic morphology of oligodendrocyte-type 2-astrocyte (O2A) progenitors or mature oligodendrocytes. One would have been motivated to isolate these cells as a means of understanding how multipotent neuroepithelial stem cells become restricted to the various neuroepithelial derivatives and in order to understand neuroepitheal

disorders in human and to treat neurological disorders in mammals, particularly humans and the treatment of certain diseases, e.g. Parkinson's Disease, are evidence of the existence of an intermediate between cell type 14 and cell type 18 of Figure 1. As stated by Rao et al., the pattern of antigen expression further suggests the existence of a dividing oligodendrocyte precursor that subsequently generates oligodendrocytes, as has been described from spinal cord cultures from older embryos. The expectation of success is high based upon the high degree of knowledge in the art and the results and expertise of Rao et al. who demonstrate the successful isolation of various cell types along the neuroepitheal development pathway.

For these reasons, claims 25, 26 and 29-41 remain rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Rao et al. (U.S. Patent No. 6,361,996 B1).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

rgh
12/17/2009

/Richard G Hutson/
Primary Examiner, Art Unit 1652